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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : A61K 9/70

A1

(11) International Publication Number: WO 93/25196

(43) International Publication Date: 23 December 1993 (23.12.93)

(21) International Application Number: PCT/US93/05487

(22) International Filing Date: 9 June 1993 (09.06.93)

(30) Priority data:
07/895,589 9 June 1992 (09.06.92) US

(60) Parent Application or Grant
(63) Related by Continuation
US 07/895,589 (CIP)
Filed on 9 June 1992 (09.06.92)

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(81) Designated States: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: METHODS FOR TREATING NON-SUTURABLE WOUNDS BY USE OF CYANOACRYLATE ADHESIVES

(57) Abstract

A cyanoacrylate adhesive is applied to non-suturable, non-sterile wound surfaces to protect and/or treat such surfaces, to promote wound healing and to retard infection of the wound.

METHODS FOR TREATING NON-SUTURABLE WOUNDS BY USE OF CYANOACRYLATE ADHESIVES

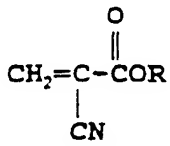
BACKGROUND OF THE INVENTION

Field of the Invention

This invention is directed to methods for treating non-suturable wounds by using cyanoacrylate adhesives. The cyanoacrylate adhesive to be used can be stored in dispensers for single or repeated/intermittent use.

State of the Art

Cyanoacrylate adhesives have been suggested for a variety of adhesive purposes including glues and surgical adhesives. In particular, cyanoacrylate adhesives of formula I:



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wherein R is an alkyl or other suitable substituents are disclosed in U.S. Patents Nos. 3,527,224; 3,591,676; 3,667,472; 3,995,641; 4,035,334; and 4,650,826. Typically, when used as adhesives for living tissues, the R substituent is alkyl of from 2 to 6 carbon atoms and most often is butyl (e.g., n-butyl).

The suggested medical uses for cyanoacrylate adhesives have apparently been limited to surgical environments wherein the cyanoacrylate adhesive is utilized, e.g., as an alternative to sutures or as a hemostat and, as such, are necessarily employed in a sterile environment. See, for example, Halpern, U.S. Patent No. 3,667,472, and Robertson, et al., U.S.

Patent No. 3,722,599. In such surgical environments, the cyanoacrylate adhesive is applied to the soft tissue under sterile conditions and, in the presence of water or protein found in soft tissue, the adhesive bonds to the skin as well as polymerizes which, in the case of adhesive sutures, joins the separated sections of soft skin tissue together.

Contrarily, most small wounds are neither treated in a surgical setting nor in a sterile environment. In a typical home setting, small wounds are generally cleaned and are either left exposed (generally if not bleeding) or are covered with a bandage (generally the case where minor bleeding occurs or where there is irritation). In either case, the wound is usually left to heal on its own over time with the accompanying discomfort during this period.

SUMMARY OF THE INVENTION

This invention is drawn to methods for treating and/or protecting small superficial wounds, i.e., non-suturable wounds, including small cuts and abrasions. The method involves applying a cyanoacrylate adhesive, particularly, n-butyl cyanoacrylate adhesive, onto the wound and allowing the adhesive to polymerize.

In the case of cuts, the cyanoacrylate adhesive is generally applied between the separated skin defining the cut as well as over the cut. The cyanoacrylate adhesive is allowed to polymerize so as to both bind the separated skin sections and form a polymer layer over the cut. In addition to serving as a protective layer, the polymer layer also serves to promote healing and to retard infection of the cut.

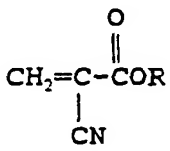
In the case of abrasions, the cyanoacrylate adhesive is generally applied over the abrasion. The cyanoacrylate adhesive is allowed to polymerize so as to form a polymer layer over the abrasion. The polymer layer serves to act as a protective layer which prevents further aggravation to the abrasion while also promoting healing and retarding infection of the abrasion.

Accordingly, in one of its method aspects, this invention is directed to a method for treating and/or protecting non-suturable superficial wounds in a non-sterile environment which wounds are characterized as superficial cuts or abrasions of less than about 0.5 centimeters in depth and from about 0.2 centimeters to about 20 centimeters in length, wherein said method comprises:

applying to said wound, in a non-sterile environment, a sufficient amount of a cyanoacrylate adhesive so as to cover the entire wound area; and

polymerizing the cyanoacrylate adhesive so as to join separated skin sections and/or to form an adhesive coating which adheres to the area where the adhesive was applied,

wherein the cyanoacrylate, in monomeric form, is represented by formula I:



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where R is selected from the group consisting of:

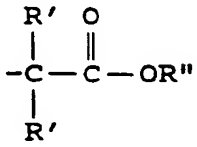
alkyl of 2 to 10 carbon atoms,

alkenyl of 2 to 10 carbon atoms,

cycloalkyl groups of from 5 to 8 carbon atoms,

phenyl,

2-ethoxyethyl,
3-methoxybutyl,
and a substituent of the formula:



wherein each R′ is independently selected from the group consisting of:
hydrogen and methyl, and
R" is selected from the group consisting of:
alkyl of from 1 to 6 carbon atoms,
alkenyl of from 2 to 6 carbon atoms,
alkynyl of from 2 to 6 carbon atoms,
cycloalkyl of from 3 to 8 carbon atoms,
aralkyl selected from the group consisting of benzyl, methylbenzyl and phenylethyl,
phenyl, and
phenyl substituted with 1 to 3 substituents selected from the group consisting of hydroxy, chloro, bromo, nitro, alkyl of 1 to 4 carbon atoms, and alkoxy of from 1 to 4 carbon atoms.

Preferably R is alkyl of from 2 to 10 carbon atoms and more preferably alkyl of from 2 to 6 carbon atoms. Most preferably, R is n-butyl.

In another of its method aspects, this invention is directed to a method for treating and/or protecting superficial non-suturable wounds in a non-sterile environment which wounds are characterized as superficial cuts or abrasions of less than about 0.1 centimeters in depth and from about 0.2 centimeters to

about 20 centimeters in length, wherein said method comprises:

applying to said wound a sufficient amount of n-butyl cyanoacrylate adhesive to cover the entire wound area; and

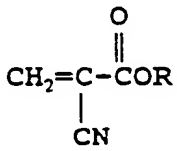
polymerizing the cyanoacrylate adhesive so as to join separate skin sections and/or to form an adhesive coating which adheres to the area where the adhesive was applied.

In a preferred embodiment, the cyanoacrylate is applied at a rate of at least 0.02 milliliter (ml), and preferably from about 0.02 to about 0.5 ml, of cyanoacrylate adhesive per square centimeter of skin which is to be covered.

In another preferred embodiment, the cyanoacrylate adhesive to be applied to the skin has a viscosity of from about 2 to about 100 centipoise at 20°C. More preferably, the cyanoacrylate adhesive is in monomeric form and has a viscosity of from about 2 to about 20 centipoise at 20°C.

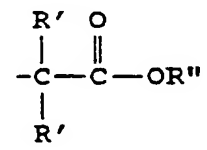
As used herein, the following terms have the following meanings:

The term "cyanoacrylate adhesive" refers to adhesive formulations based on cyanoacrylate monomers of formula I:



I

where R is selected from the group consisting of alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 20 carbon atoms, cycloalkyl groups of from 5 to 8 carbon atoms, phenyl, 2-ethoxyethyl, 3-methoxybutyl, and a substituent of the formula:



where each R′ is independently selected from the group consisting of hydrogen and methyl and R" is selected from the group consisting of alkyl of from 1 to 6 carbon atoms; alkenyl of from 2 to 6 carbon atoms; alkynyl of from 2 to 6 carbon atoms; cycloalkyl of from 3 to 8 carbon atoms; aralkyl selected from the group consisting of benzyl, methylbenzyl and phenylethyl; phenyl; and phenyl substituted with 1 to 3 substituents selected from the group consisting of hydroxy, chloro, bromo, nitro, alkyl of 1 to 4 carbon atoms, and alkoxy of from 1 to 4 carbon atoms.

Preferably, R is an alkyl group of from 1-10 carbon atoms including methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, n-pentyl, iso-pentyl, n-hexyl, iso-hexyl, 2-ethyl-hexyl, n-heptyl, octyl, nonyl, and decyl. More preferably, R is butyl and most preferably, R is n-butyl.

These cyanoacrylate adhesives are known in the art and are described in, for example, U.S. Patent Nos. 3,527,224; 3,591,676; 3,667,472; 3,995,641; 4,035,334; and 4,650,826 the disclosures of each are incorporated herein by reference in their entirety.

A preferred cyanoacrylate adhesive for use in the invention is n-butyl-2-cyanoacrylate.

The cyanoacrylate adhesives described herein rapidly polymerize in the presence of water vapor or tissue protein, and the n-butyl-cyanoacrylate capable of bonding human skin tissue without causing histoxicity or cytotoxicity.

The term "non-suturable or small wounds" means superficial cuts and abrasions, generally less than about 0.5 cm in depth and preferably less than about 0.1 cm in depth and of varying lengths although generally ranging from about 0.2 cm to about 20 cm in length and preferably 0.2 cm to about 10 cm in length. Such superficial wounds include cuts where the skin is separated and can be joined together, as well as abrasions such as "nicks" or "scrapes" where the skin is removed. However, non-suturable wounds do not include puncture wounds.

In general, the length of an abrasion is taken as the longest possible line defined by the abrasion and, accordingly, the width of any abrasion is necessarily less than the length of the abrasion.

In view of the above, non-suturable wounds as defined herein include common cuts and scratches which rarely need medical attention unless located in a sensitive area or unless secondary infection occurs. As opposed to the edges of suturable wounds which can be widely separated, the edges of non-suturable wounds can easily be opposed or brought together. One particular example of a non-suturable wound treatable by the methods of this invention is skin tearing adjacent the site of a catheter implant.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

This invention relates to cyanoacrylate adhesives which are useful for treating and/or protecting superficial non-suturable wound surfaces. The adhesive is useful for treating wounds in an every day, typical non-sterile environment.

The cyanoacrylate adhesive to be applied to wound surfaces can be monomeric or partially polymeric. In general, partially polymerized cyanoacrylate adhesives are liquid polymers having a higher viscosity than that of the corresponding monomer and, therefore, are better suited for those applications which are intended to be specific for a particular skin area. In other words, less viscous materials are more likely to "run" (i.e., flow) into areas where application was not intended.

The cyanoacrylate adhesives used herein preferably have a viscosity of from about 2 to about 100 centipoise and more preferably from about 2 to about 20 centipoise at 20°C. The specific viscosity of the formulation depends on the amount and degree of partially polymerized cyanoacrylate adhesive employed. Such factors are readily ascertainable by the skilled artisan. For example, methods for preparing partially polymerized cyanoacrylate adhesives are disclosed, for example, by Rabinowitz, U.S. Patent No. 3,527,224 which is incorporated herein by reference in its entirety.

Monomeric forms of cyanoacrylate adhesives are often preferred where application is to be made to a large surface. This preference results from the fact that those forms are less viscous and, accordingly, will permit more facile large surface area application.

Mixtures of monomeric forms of cyanoacrylate adhesive and partially polymerized forms of cyanoacrylate adhesive can also be used to prepare a formulation having intermediate viscosities.

For purposes of this invention, monomeric or partially polymerized n-butyl-2-cyanoacrylate is a particularly preferred adhesive and is capable of effectively bonding human tissues without causing histoxicity or cytotoxicity.

Upon contact with skin moisture and tissue protein, the cyanoacrylate adhesives will polymerize or, in the case of partially polymerized cyanoacrylate adhesives, will further polymerize, at ambient conditions (skin temperature) over 10 seconds to 60 seconds to provide a solid layer which forms over and strongly adheres to the surface of the skin, thus providing a protective layer to the wound area.

The adhesive is applied to provide an effective thick coating over living tissue without diffusing into the tissue in amounts to cause irritation or necrosis of the tissue. Generally, the adhesive provides an adhesive film coating over the wound area which when set is satisfactorily flexible and adherent to the tissue without peeling or cracking. Preferably, the adhesive coating has a thickness of less than about 0.5 millimeter (mm), and more preferably the coating has a thickness of less than about 0.3 mm. In a particularly preferred embodiment, the thickness of the adhesive coating is from about 0.1 millimeter to about 0.5 millimeter and even more preferably from about 0.1 millimeter to about 0.3 millimeter.

The adhesive coating can also be formed by applying at least about 0.02 ml of cyanoacrylate adhesive per square centimeter of skin and more preferably from about 0.02 to about 0.5 ml of cyanoacrylate adhesive per square centimeter of skin and even more preferably from about 0.02 to about 0.05 ml of cyanoacrylate adhesive per square centimeter of skin.

The cyanoacrylate adhesive coating provides an airtight, waterproof seal around the wound which does not need to be replaced when the wound gets wet. Once applied, the coating prevents bacterial and contaminant entry into the wound, thus reducing the rate of secondary infection. Generally, the adhesive coating does not limit dexterity and promotes faster wound healing.

FORMULATIONS

The cyanoacrylate adhesive formulations employed herein generally comprise monomeric and/or partially polymerized compounds of formula I described above. These formulations are liquid in nature and, upon contact with skin moisture, will polymerize to provide a solid film or layer over the skin surface.

The formulations may additionally contain one or more optional additives such as colorants, perfumes, anti-diffusion agents, modifying agents and stabilizers. In practice, each of these optional additives should be both miscible and compatible with the cyanoacrylate adhesive. Compatible additives are those that do not prevent the use of the cyanoacrylate adhesives for their intended use.

In general, colorants are added so that the polymerized film will contain a discrete and discernable color. Perfumes are added to provide a pleasant smell to the formulation. Stabilizers are added to minimize in situ polymerization in containers during storage. Each of these additives is conventional. For example, suitable stabilizers are disclosed in U.S. Patent No. 4,650,826 the disclosure of which is incorporated herein by reference in its entirety.

The formulation is generally stored in an applicator for use in a single dose application or for use in repeated applications. Single dose applicators include those having breakable or removable seals that prevent moisture, including atmospheric moisture, from contacting the formulation and causing in situ polymerization.

For repeated and intermittent usage, minimal exposure to atmospheric moisture is required. This can be achieved by devices having very narrow outlets and low initial deadspace. One applicator for such repeated intermittent use is described in U.S. Patent No. 4,958,748 which is incorporated herein by reference.

A preferred applicator for repeated and intermittent usage is an applicator suitable for the non-sterile storage and metered dispensement of a cyanoacrylate adhesive after opening of the applicator wherein the applicator is characterized as having a resealable opening of no more than about 0.25 square inch (1.613 square centimeters) so as to permit the metered dispensement of the adhesive from the applicator and which is capable of multiple

administrations of the adhesive and is further characterized as having resealing means such as a cap which either tightly mates with the applicator or which screws onto the applicator.

Preferably, the opening of the applicator is about 0.001 to about 0.10 square inch (about 0.00645 to about 0.645 square centimeters).

In another preferred embodiment, the walls of the applicator are made of a pliable material, so that upon application of pressure onto the walls, the walls depress sufficiently to force the adhesive contained in the applicator through the opening. Preferably, the applicator is manufactured with its opening covered by a metal foil or other similar construction which closes this opening until the device is ready for use. The opening is then reinstated by use of a pin or similar device which punctures the covering.

In applicators suitable for repeated intermittent uses, the cyanoacrylate adhesive is stored at ambient conditions and is selected to be bacteriostatic. See, for example, Rabinowitz et al., U.S. Patent No. 3,527,224. When the selected adhesive is bacteriostatic, prolonged storage at ambient conditions is without regard to the sterility of the formulation because there is no adverse buildup of bacteria during storage.

METHODOLOGY

The above-described formulations are applied to a wound area under conditions suitable for polymerizing the adhesive so as to form a protective coating. In general, the wound is usually first

cleaned (soap/water and optionally a disinfectant), and then sufficient amounts of cyanoacrylate adhesive are employed to cover or encase the entire scrape, scratch or nick area. For cuts, an amount sufficient to join the opposing skin edges is applied, and optionally a sufficient amount is applied to also encase the entire cut area. For scrapes, a sufficient amount is applied to encase the entire wound area.

When the adhesive is applied to cover or encase the wound area, sufficient cyanoacrylate adhesive is preferably employed to form a coating of less than about 0.5 mm thick and more preferably at least about 0.1 mm thick. Such coatings are formed by applying at least about 0.02 ml of cyanoacrylate adhesive per square centimeter of skin surface area.

The amount of cyanoacrylate adhesive applied onto the skin surface area can be controlled by the amount of adhesive packaged in a single dose product or by use of a multiple use dispenser which governs the amount of material applied onto the skin. In this regard, the dispenser described by Otake, U.S. Patent No. 4,958,748, which is incorporated by reference in its entirety, is particularly advantageous because it dispenses the adhesive in a controlled dropwise manner.

Upon application of the cyanoacrylate adhesive, the surface skin moisture, tissue protein, and temperature are sufficient to initiate polymerization of the adhesive upon application. Thereafter, the skin surface is maintained under suitable conditions to allow polymerization to proceed to formation of an adhesive coating.

In general, the particular length of time required for polymerization will vary depending on factors such as the amount of adhesive applied, the temperature of the skin, the moisture content of the skin, the surface area of the wound, and the like. However, in a preferred embodiment, polymerization is generally complete within about 10 seconds to about 60 seconds while the skin is maintained at ambient conditions. During this period, the person to whom application of the cyanoacrylate adhesive has been made merely allows the adhesive to form a coating while minimizing any action to prevent the adhesive from being dislodged from that portion of the skin where it was applied or to adhere to unintended objects. After the adhesive coating has formed, the coating strongly adheres to the skin, is flexible and waterproof, thereby protecting the wound area and promoting healing.

It is important to note that the adhesive coating of the invention can be applied in a non-sterile environment to a non-sterile surface. This is directly contrary to the use of cyanoacrylates as surgical adhesives which requires one-time use in a sterile environment. The invention provides for storage of the adhesive in a dispenser for repeated intermittent uses in a non-sterile environment.

In general, the coating will adhere to the skin for a period of about 2-3 days after which time it sloughs off. Additional applications can be made if desired.

The coating protects non-suturable wounds because the adhesive forms a polymer coating which extends over the entire surface of the wound to protect

the wound in much the way a bandage does while, in the case of cuts, also joins together the separated skin surfaces.

One particular example of a non-suturable wound treatable by the methods of this invention is skin tearing adjacent the site of a catheter implant. Specifically, it is common after catheter implantation to have the skin adjacent the catheter to tear, partly from catheter movement relative to the site of catheter implantation due to the patient's muscle contractions, etc. Such tears are typically non-suturable wounds to the extent that they are less than 0.5 centimeter deep and from about 0.2 to about 20 centimeters in length, Such tears can become the site of infection and are prone to further tearing. Moreover, as the skin tears adjacent a catheter implant, it becomes difficult to maintain the catheter in the implant site. Heretofore, there were no acceptable methods to treat such tearing and potentially inadvertent catheter removal other than to reinsert the catheter at another site.

The methods of this invention now provide for a method to treat such tearing without removal of the catheter. Specifically, in this particular aspect of the methods of this invention, the cyanoacrylate adhesive is applied onto these tears and then polymerized as described generally above. This results in joining the separated skin sections of the tear which protects the tear and retards further tearing thereof.

This method can also be employed prophylactically by applying the cyanoacrylate adhesive to the skin areas adjacent the cathether prior to actual skin tearing. In this regard, application is

generally made in the manner and amounts described above and is preferably applied to the skin area approximately 1 centimeter and preferably about 0.5 centimeter in diameter around the cathether implant.

Accordingly, this aspect of the present invention is directed to a method for retarding skin tearing adjacent a catheter implant which method comprises:

applying a sufficient amount of a cyanoacrylate adhesive so as to cover an untorn skin area adjacent a catheter implant; and

polymerizing the cyanoacrylate adhesive so as to form a polymer film over the skin area which film adheres to the skin area where the adhesive was applied,

wherein the cyanoacrylate adhesive, in monomeric form, is represented by formula I as described above.

In the above prophylactic methods, the polymer film or coating is preferably less than about 0.5 millimeter in thickness and more preferably from about 0.1 to about 0.5 millimeter in thickness and still more preferably, from about 0.1 to about 0.3 millimeter in thickness.

Whether employed prophylactically or to treat existing tears, care should be taken during application of the cyanoacrylate adhesive to the skin areas adjacent catheter implantation to ensure against penetration of the adhesive into the skin puncture defined by the catheter so as to avoid skin irritation. One method for avoiding such penetration of the adhesive is to employ a viscous cyanoacrylate adhesive formulation preferably having a viscosity of from about

40 to about 100 centipoise at 20°C. Such viscous formulations tend to remain at the site of application and not run into the puncture wound. Moreover, a colorant can be incorporated into the cyanoacrylate adhesive composition to readily discern where the adhesive has been applied.

Still another particular example of a non-suturable wound treatable by the methods of this invention is the superficial skin tearing remaining after suture removal. Typically, in the case of suturable wounds (e.g., surgical wounds), the separated skin sections are joined by either sutures or by staples (collectively "sutures"), and the wound typically heals outward. That is to say that the internal sections of the wound heal first with subsequent healing outward to the skin surface. Accordingly, when the sutures are removed, the remaining wound is typically a superficial non-suturable wound because the non-healed portions of the original wound are less than 0.5 centimeter in depth and are typically less than about 20 centimeters in length. In this regard, application of the cyanoacrylate adhesive to these wounds after suture removal as per the methods described herein provides an effective method to treat these wounds. Additionally, when the adhesive is applied to form an adhesive coating over the wound, the resulting coating is waterproof and flexible thereby allowing the patient significant freedom in bathing, swimming, etc. as compared to current practice after suture removal where the patient is instructed to minimize water contact with the wound for several days.

The following example illustrates certain embodiments of the invention but is not meant to limit the scope of the claims in any way.

Example 1

A cyanoacrylate adhesive formulation was prepared in monomeric form using n-butyl α-cyanoacrylate. The formulation was placed into the dispensing device described by Otake, U.S. Patent No. 4,958,748.

One drop of such a formulation is placed dropwise onto the skin of a finger having a paper cut of about 0.05 centimeter in depth and about 3 centimeters in length. About 30 seconds is allowed for polymerization of the adhesive. At which time, the separated skin areas defining the cut are both joined and encased by a polymer coating.

From the foregoing description, various modifications and changes in the composition and method will occur to those skilled in the art. All such modifications coming within the scope of the appended claims are intended to be included therein.

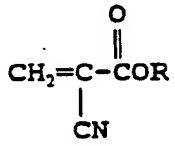
WHAT IS CLAIMED IS:

1. A method for treating and/or protecting non-suturable wounds in a non-sterile environment which wounds are characterized as superficial cuts or abrasions of less than about 0.5 centimeter in depth and from about 0.2 centimeter to about 20 centimeters in length, wherein said method comprises:

applying to said wound, in a non-sterile environment, a sufficient amount of a cyanoacrylate adhesive so as to cover the entire wound area; and

polymerizing the cyanoacrylate adhesive so as to join separated skin sections and/or to form an adhesive coating which adheres to the area where the adhesive was applied,

wherein the cyanoacrylate adhesive, in monomeric form, is represented by formula I:



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where R is selected from the group consisting of:

alkyl of 2 to 10 carbon atoms,

alkenyl of 2 to 10 carbon atoms,

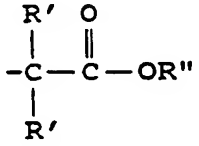
cycloalkyl groups of from 5 to 8 carbon atoms,

phenyl,

2-ethoxyethyl,

3-methoxybutyl,

and a substituent of the formula:



wherein each R′ is independently selected from the group consisting of:

hydrogen and methyl, and

R" is selected from the group consisting of:

alkyl of from 1 to 6 carbon atoms,

alkenyl of from 2 to 6 carbon atoms,

alkynyl of from 2 to 6 carbon atoms,

cycloalkyl of from 3 to 8 carbon atoms,

aralkyl selected from the group consisting of benzyl, methylbenzyl and phenylethyl,

phenyl, and

phenyl substituted with 1 to 3 substituents selected from the group consisting of hydroxy, chloro, bromo, nitro, alkyl of 1 to 4 carbon atoms, and alkoxy of from 1 to 4 carbon atoms.

2. A method according to Claim 1 wherein R is alkyl of from 2 to 6 carbon atoms.

3. A method according to Claim 2 wherein R is butyl.

4. A method according to Claim 3 wherein R is n-butyl.

5. A method according to Claim 1 wherein the non-suturable wound is a skin tear adjacent the site of a catheter implant.

6. A method according to Claim 4 wherein the non-suturable wound is a skin tear adjacent the site of a catheter implant.

7. A method according to Claim 5 wherein the cyanoacryalate adhesive has a viscosity of from about 40 to ab ut 100 centipoise at 20°C.

8. A method according to Claim 6 wherein the cyanoacrylate adhesive has a viscosity of from about 40 to about 100 centipoise at 20°C.

9. A method for treating and/or protecting superficial non-suturable wounds in a non-sterile environment which wounds are characterized as superficial cuts or abrasions of less than about 0.1 centimeter in depth and from about 0.2 centimeter to about 20 centimeters in length, wherein said method comprises:

applying to said wound a sufficient amount of n-butyl cyanoacrylate adhesive to cover the entire wound area; and

polymerizing the n-butyl cyanoacrylate so as to join separate skin sections and/or to form an adhesive coating which adheres to the area where the adhesive was applied.

10. A method according to Claim 9 wherein said adhesive is applied to said wound at an amount of at least 0.02 ml of cyanoacrylate adhesive per square centimeter of skin which is to be covered.

11. A method according to Claim 1 wherein the cyanoacrylate adhesive has a viscosity of from about 2 to about 100 centipoise at 20°C.

12. A method according to Claim 11 wherein the cyanoacrylate adhesive has a viscosity of from about 2 to about 20 centipoise at 20°C.

13. A method according to Claim 9 wherein the cyanoacrylate adhesive has a viscosity of from about 2 to about 100 centipoise at 20°C.

14. A method according to Claim 13 wherein the cyanoacrylate adhesive has a viscosity of from about 2 to about 20 centipoise at 20°C.

15. A method according to Claim 1 wherein the cyanoacrylate adhesive is applied at a concentration of at least 0.02 ml per square centimeter.

16. A method according to Claim 9 wherein the cyanoacrylate adhesive is applied at a concentration of from about 0.02 ml to about 0.05 ml per square centimeter.

17. A method according to Claim 1 wherein the cyanoacrylate adhesive is applied from a single use applicator.

18. A method according to Claim 1 wherein the cyanoacrylate adhesive is applied from a multiple, intermittent use applicator.

19. A method according to Claim 1 wherein the non-suturable wound is a superficial skin tear remaining after removal of sutures.

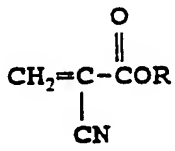
20. A method according to Claim 19 wherein the cyanoacrylate adhesive forms an adhesive coating over the wound.

21. A method for retarding skin tearing adjacent a catheter implant which method comprises:

applying a sufficient amount of a cyanoacrylate adhesive so as to cover an untorn skin area adjacent a catheter implant; and

polymerizing the cyanoacrylate adhesive so as to form a polymer film over said skin area which film adheres to the area where the adhesive was applied,

wherein the cyanoacrylate adhesive, in monomeric form, is represented by formula I:



I

where R is selected from the group consisting of:

alkyl of 2 to 10 carbon atoms,

alkenyl of 2 to 10 carbon atoms,

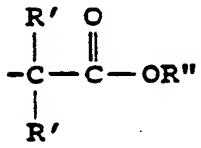
cycloalkyl groups of from 5 to 8 carbon atoms,

phenyl,

2-ethoxyethyl,

3-methoxybutyl,

and a substituent of the formula:



wherein each R′ is independently selected from the group consisting of:

hydrogen and methyl, and

R" is selected from the group consisting of:

alkyl of from 1 to 6 carbon atoms,

alkenyl of from 2 to 6 carbon atoms,

alkynyl of from 2 to 6 carbon atoms,

cycloalkyl of from 3 to 8 carbon atoms,

aralkyl selected from the group consisting of benzyl, methylbenzyl and phenylethyl,

phenyl, and

phenyl substituted with 1 to 3 substituents selected from the group consisting of hydroxy, chl ro, bromo,

nitro, alkyl of 1 to 4 carbon atoms, and alkoxy of from 1 to 4 carbon atoms.

22. A method according to Claim 21 wherein the cyanoacrylate adhesive has a viscosity of from about 40 to about 100 centipoise at 20°C.

23. A method according to Claim 22 wherein the cyanoacrylate adhesive composition comprises n-butyl cyanoacrylate.

INTERNATIONAL SEARCH REPORT

Int...ational application No.
PCT/US93/05487

A. CLASSIFICATION OF SUBJECT MATTER
IPC(5) :A61K 9/70
US CL :424/445
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/445, 443, 446, 447, 404, 487, 78.07, 78.31

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US, A, 3,527,224 (RABINOWITZ) 08 SEPTEMBER 1970, SEE ENTIRE DOCUMENT.	1-4,7-11,13 15-20 1-23
Y	ARCH. SURG. VOL. 93, SEPT. 1966 (LEHMAN)"TOXICITY OF ALKYL 2-CYANOACRYLATES", SEE PAGES 447-450.	1-23

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be part of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 16 AUGUST 1993	Date of mailing of the international search report 23 SEP 1993
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. NOT APPLICABLE	Authorized officer NEIL LEVY Telephone No. (703) 308-2351

Form PCT/ISA/210 (second sheet)(July 1992)*